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Future Directions for Pediatric Obesity Treatment

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There has been an increasing body of research on methods to treat pediatric obesity. This literature has been thoroughly reviewed (1-4), with the majority of reviews optimistic about the effectiveness of pediatric obesity treatments. Our laboratory has generated a large number of randomized trials designed to treat pediatric obesity (5), with research showing that the effects of obesity treatments can be sustained for many years after cessation of treatment, and the effects of current treatments are more powerful than those developed over 25 years ago, despite children being more obese and the environment more obesiogenic (6). The family-based treatment approach to pediatric obesity has been replicated many times (7-9), including replication of long-term benefits (8). We believe that the family-based treatment approach should be considered as a work in progress, rather than a static treatment, and as investigators develop a better understanding of ways to change behavior, and factors that influence child eating and activity, more powerful treatments should evolve (5). Although there has been much progress in the field of pediatric obesity treatment, the prevalence of the problem remains a concern. More research is needed to treat children who are overweight, and at risk for becoming overweight adults with comorbidities associated with obesity. Because there has been a number of reviews of pediatric obesity treatment studies (1-4), the goal of this commentary is to present new directions to guide the development of the next generation of pediatric obesity efforts. The commentary will be divided into sections on treatment development and treatment evaluation.

TREATMENT DEVELOPMENT

The role of basic science in treatment development

One of the most often expressed clinical research needs is translation of basic science into clinical interventions. The National Institutes of Health have made translational research a priority, providing funding for the development of clinical and translational research centers in medical schools. Consistent with this effort, the National Institutes of Health have solicited applications for Center grants to translate basic behavioral science into clinical interventions for obesity. These funding efforts acknowledge the importance of basic research as a stimulus for clinical interventions, but the need to develop funding for these centers suggests there has not been sufficient emphasis on translating basic science into clinical interventions for obesity. There is a wealth of basic findings that can be developed into clinical interventions. We will highlight several promising directions. We view basic science quite broadly, and do not abide by the idea that basic science needs to be molecular, but good basic science can be studied at multiple levels. Basic research attempts to derive principles that can lead to treatment applications across a broad range of levels of analysis.

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Molecular genetics—Genetics represent an individual difference variable that can influence behavior. An important contemporary area in biomedical research designed to understand how genetic polymorphisms are related to drug effects is pharma-cogenetics (10). It would not be surprising if behavioral interventions also were differentially effective based on genetics, and behavioral–genetic interactions are discovered that help to predict who will respond to specific types of treatments. There is progress being made that relates specific genotypes to behavioral phenotypes that are related to energy balance. For example, Wardle and colleagues have shown that polymorphisms of the *FTO* gene, that has been related to obesity in multiple samples, influences eating and satiety in children (11,12). Differences in treatment effectiveness may be related to genetic factors such as polymorphisms of the *FTO* gene.

Basic behavioral science—Most pediatric obesity treatment studies acknowledge the use of behavioral treatments or base their treatments on behavioral science theories, such as cognitive behavioral theory. However, clinical investigators are often unaware of new breakthroughs in basic behavioral science that can inform the development of new treatments. An excellent example of a relatively neglected research area that could advance treatment development is Bouton's work on context specific extinction (13,14). A view commonly held in behavior therapy is that when a behavior is extinguished and a new behavior is learned that the old behavior is gone from the repertoire. Bouton's work clearly shows that the behavior is under the control of the context in which it was learned, and is always ready to emerge when the conditions that gave birth to the old behavior are returned to, which often happens when treatment is completed and behavior relapses. An exciting new development in application of basic science to clinical interventions that extends Bouton's ideas is research suggesting that memories, and thus conditioned responses, are not permanent, but go through a process of reconsolidation when a memory is retrieved, and careful use of extinction during the reconsolidation window may attenuate retrieval of memories (15). Because conditioned food cravings are so important to eating, the development of new treatments that permanently alter these cravings would have important applications to pediatric obesity treatments. Many investigators have theorized that the acquisition and maintenance of behavior are regulated by different processes, and new work by Fuglestad *et al*. (16) suggest that approach (or promotion) focused goals may be more effective during initiation/treatment phase of an intervention, but that avoidance (or prevention) focused goals are more effective during maintenance. This may take advantage of the importance of risk aversion in maintaining behavior, in that people may be more motivated to avoid losing something they have then in obtaining something new. These are exciting examples of theory driven research on relapse and the conditions that foster behavior maintenance, and this is an area for future study.

Educational science—Treatments for pediatric obesity attempt to teach children, parents, and family members new ways to eat or be physically active. The education can take different forms, ranging from individual or group visits, to internet or printed self-help materials. Despite the central role of education, there is very limited research on the best way to teach families about eating and exercise, and how to change behavior. In most clinical environments therapists have adopted a structure for treatment implementation based on convenient meeting times and intervals, like weekly during the initial stages of treatment, shifting to longer intervals, until the treatment is faded out entirely. Is the ideal interval for teaching new behaviors weekly, and is the ideal amount of time 1 h/week?

The use of the best educational technologies to promote learning and behavior change is almost a totally neglected area. The majority of treatment protocols are implemented using a structured lesson plan, in which new information is introduced each session, independent of whether participants have learned the previous information. Because people learn and change behavior at different rates, mastery programs that take these individual differences into account may tailor the programs better to each person's learning schedules (17). There is a revolution

occurring in educational science in which educators are working to translate basic learning and cognitive science into new teaching techniques to improve learning (18). A simple promising technique is increasing the amount of testing during learning, as this increases both learning and long-term retention. Many obesity treatment programs do not test families on the material presented. Although not testing families reduces the burden on families, this may inadvertently compromise learning opportunities.

Developmental sciences—Developing treatments for childhood obesity is not a unitary matter. Infants, toddlers, preschoolers, elementary school children, preadolescents, early and late adolescents may be obese, and different treatments may be needed for each of these levels. Children differ in their cognitive abilities, capacities for self-regulation, social networks and how they respond to parents, teachers, and friends/peers. The majority of research has been made with preadolescent and adolescent children. But very little of this research has been informed by developmental data on acquisition of habits, differences in cognitive abilities, and the use of different materials and teaching techniques tailored to the different abilities and influences on children based on their developmental level.

Decision sciences—Overweight children value food more and are more motivated to eat and value activity less and are less motivated to be active than leaner peers (19,20). In addition, obese children may find it harder to delay gratification associated with food than leaner peers (21,22). Obese persons may have memory biases that favor attending to food cues (23,24), and an innovative theory argues that individual differences in memory are critical for the development of obesity (25). Obesity is related to loss of cognitive function in adults (26), and recent research suggests that pediatric obesity may also set the stage for cognitive impairment and challenges in executive function (27). Making behavior changes can be a complicated business for adults, and maybe more so for children. It may be even harder for someone who overvalues the behaviors that need to be reduced, is impulsive, has trouble inhibiting unhealthy behaviors, and who has deficits in executive functioning. These examples of how reinforcing value or impulsivity influence choice or eating and activity are examples of behavioral economics. Behavioral economics goes beyond traditional choice models that focus on rational decision making to include nonrational aspects of decision making, such as impulsivity or risk aversion. The interest in behavioral economics has also revived interest in use of financial incentives for behavior change and weight loss (28), which has been an important addition to treatment of drug abuse (29) and may become important in treating obesity. An interesting approach to behavior change derived from behavioral economics is asymmetric paternalism, which focuses on noncoercive ways to facilitate healthier choices that can be applied at the societal or individual levels (30). There are many ways in which asymmetric paternalism could be applied to changing children's eating behaviors, such as schools providing youth with chilled water as the default drink with lunch, putting snack foods under counter so kids have to ask for them, or moving vending machines to less accessible locations. A noncoercive way to increase physical activity would be to put children's classes in very different parts of a school, such that children would have to get a substantial amount of activity just in the process of going to class. It may be worthwhile to consider including standard approaches to reducing impulsivity and improving executive functioning as components of obesity treatment programs.

Social networks—One of the biggest recent social science discoveries was that social networks influence obesity (31), with the message that obesity spreads among those in the network. Though the general phenomenon is not surprising, there have been limited attempts to take advantage of the idea of social networks, and the mechanisms that may control the influence of social networks on behavior. Many pediatric obesity treatments include information for other family members, and many also target behavior change in multiple family

members. But to our knowledge, few include friends as part of the social network to modify healthy behaviors. One exception by Wilfley and colleagues showed that providing training in peer support improved long-term maintenance of weight loss in children with better social skills (7). Developing a clearer understanding of how social networks can be used in treating pediatric obesity may benefit the obese child. An interesting theoretical aspect of social networks is the influence of behaviors on others in the network, which suggests that the benefits of positive peer interaction may not be limited to the targeted obese child, but rather may extend to the peer helping the obese child change their behaviors, and other's in the child's social network.

Integrating interventions—Pediatric obesity interventions can be differentiated by their orientation, as a recent review has divided the approaches into dieting, lifestyle, behavioral treatments, pharmacotherapy, surgery, and intensive in-patient treatment (4). There may be advantages to integrating treatments. For example, behavioral treatments could incorporate pharmacotherapy to enhance or produce behavior change by tailoring the behavioral program to the specific effects produced by the drugs. It is notable that there have been very few studies that have combined clinical and community resources in the treatment of obesity. However, there are several prevention studies in which multiple resources have been integrated that have been shown to be effective. For example, a community-based environmental intervention that integrated groups of individuals within the school, home, and community significantly reduced child zBMI compared with children in the control condition (32). Likewise, a multicomponent school nutrition policy initiative developed and delivered by a community-based organization incorporated strategies of school staff training, nutrition policy changes, social marketing, and family outreach to prevent overweight (33). These studies illustrate the integration of clinical and community resources for obesity prevention, and could serve as potential models for structuring future treatment approaches that examine a wide range of possibilities. For example, can school or community-based teams be used to enhance exercise programs in obesity treatment? Can community recreational centers collaborate with academic centers to provide safe places for children to be active? Can after school programs be used to teach positive eating and activity to enhance the quality of clinic-based treatments? There are many possible avenues for integrating interventions at different levels that may be additive or synergistic in their effects on childhood obesity.

Public policy changes can alter the obesigenic environment, and thus interact with treatment to make it easier for obese children and their families to make behavior changes. For example, removing soda machines from schools, posting calorie information on menus, promoting walking to school, providing safe places for children to exercise, increasing time for physical education, taxing "junk" foods or subsidizing fruits and vegetables, and providing easier ways to understand nutritional information using signposting or point of purchase information are commonly discussed methods to alter the environment for children. Given the potential reach of these programs, they are worth evaluating to determine whether they interact with different types of treatments to influence obesity outcomes.

Embrace variability—All pediatric obesity treatments are associated with variability in outcome. Variability may arise from many sources, including differences in the methods and contexts of treatment delivery. Perhaps the main source of variability is individual differences in treatment response. This variability is generally ignored in hopes of identifying the best aggregate treatment effect. But, because children respond differently to treatment based on many variables, including gender, age, family situation, learning history, genetics, or biology, it may be useful to identify moderators of treatment outcome. For example, if a specific treatment works better for girls than boys, understanding why could lead to effective ways to adapt the treatment to boys. Future research that generates new knowledge on moderators of treatment effects could help to inform such decisions and lead to more effective treatment

approaches tailored to best match children's unique characteristics that may moderate treatment outcome.

Variability is also important in evaluating treatment (6). Treatments can differ in the amount and variability of change. Given equal variability, the preferred treatment would produce the largest zBMI change. When two treatments result in the same zBMI change but differ in variability, the treatment of choice would be the one with smaller variability. The most challenging choice is between a treatment with large effects and large variability compared with a treatment with smaller effects and low variability. In this case many people would choose the alternative with the bigger payoff, but the better choice might be the safer choice in which smaller but more reliable changes are observed.

TREATMENT EVALUATION

Effectiveness vs. efficacy

Treatment research usually proceeds from efficacy research that places a premium on internal validity and tight intervention control to effectiveness research that emphasizes external validity, or demonstrating the intervention effects in a broad sample of the population. When efficacious interventions are identified, the next step is effectiveness trials to demonstrate the public health implications of particular treatment approaches. Despite reviews suggesting a strong evidence base for several pediatric obesity treatments, to our knowledge there have been no effectiveness trials.

Effectiveness trials can differ from efficacy trials in a number of ways. The subjects may be more representative of the general population than subjects carefully screened for an efficacy trial. The therapists implementing the study may differ in training level and general interest in treatment evaluation in comparison with therapists in an academic setting. Finally, most efficacy trials take place in academic settings, while an effectiveness research should be implemented in the clinical or community setting in which it will be delivered. Thus, there are several factors that may influence the generalization of an efficacious treatment to a clinical or community settings, and comprehensive effectiveness research should assess the contributions of each of these factors to treatment outcome. As research is designed to translate efficacious treatments to community settings, it may be worthwhile to systematically vary one factor at a time. For example, a first step might be to test an efficacious intervention delivered by the same therapists who implemented the efficacy trial in the same setting, but with a sample more representative of the general population. These studies should be part of the next generation of treatment studies to ensure that the most powerful interventions are used in clinical settings to treat obese youth. A particularly innovative new approach to effectiveness may be using adaptive interventions, in which participants can experience a sequence of more tailored, costly, and/or labor intense interventions based on their need (34,35). Thus, some people may respond to minimal interventions, while others may need more powerful treatments, and adaptive interventions provide the opportunity for people with different needs to obtain the treatment they need.

Cost-effectiveness

One important factor that may differentiate treatments is cost-effectiveness. One way to conceptualize cost-effectiveness is to determine how much it costs to produce 1 pound of weight loss or 1 unit zBMI change, which would be used to compare weight loss treatments. A broader approach to cost-effectiveness would be to compare interventions across different health outcomes (obesity, diabetes, cancer, etc.) for the lowest cost per quality-adjusted life year (36). One potential benefit of family-based treatment, in which both the obese child and an obese parent are targeted for change, is the simultaneous improvement in multiple family

members, which may alter cost-effectiveness. For example, if a treatment that targeted only the child and a treatment that targeted both the parent (8,9) and child were equally successful for the child, but more successful for the combined parent/child dyad, then the choice of treatment might be shifted to the one in which multiple family members are targeted. The inclusion of social network theory may provide a conceptual basis for generalization of treatment effects beyond the targeted child and or parent, which could provide a new theoretical approach to evaluate cost-effectiveness research.

In assessing cost-effectiveness it is also important to consider costs from a number of viewpoints. For example, an insurance company, governmental agency, hospital, researcher, clinician, study participant, and community may be interested in assessing effectiveness in relation to the costs that most directly apply to each party. Thus, assessing cost-effectiveness using a societal approach in which direct medical and nonmedical costs and indirect costs are included could be most useful. From a societal perspective, obesity intervention costs would be assessed across multiple domains and could include direct costs of intervention delivery and health care utilization, nonmedical costs to participants that include costs associated with changes in energy intake and physical activity patterns, and indirect costs such as changes in work and leisure time as a result of the intervention (37).

Summary

The goal of this commentary was to present ideas that could help to guide the evolution of the next generation of pediatric obesity treatments. Whereas considerable progress has been made in treatment efficacy studies, there is the potential for enhancing the efficacy of existing treatments and developing new paradigms to treat pediatric obesity by tailoring treatment based on moderators of treatment success, and translating basic science into clinical interventions. It will be necessary to then evaluate efficacious treatments using effectiveness designs, and to evaluate their cost-effectiveness.

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